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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/257,272	02/25/1999	JING-SHAN HU	PF112P2D2	1980

22195 7590 08/13/2002

HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
ROCKVILLE, MD 20850

EXAMINER

LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 08/13/2002

26

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/257,272

Applicant(s)

HU ET AL.

Examiner

Robert Landsman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 May 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 33-272 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 33-272 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 22.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

1. Formal Matters

- A. Amendment C, filed 5/22/02, has been entered into the record.
- B. The Supplemental Information Disclosure Statement, filed 3/12/02, has been entered into the record.
- C. The Supplemental Information Disclosure Statement, filed 4/18/02, has been entered into the record. However, since Statutory Declarations are not proper subject matter for an IDS, Applicants have not submitted a Form PTO-1449.
- D. Claims 1 and 33-400 were pending in the application. Claims 1 and 273-400 have been canceled. Therefore, claims 33-272 are pending and are the subject of this Office Action.
- E. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Information Disclosure Statement

- A. Reference FA of Paper No. 22 has been lined through since an International Search Report is not a proper reference for an IDS.

3. Claim Rejections - 35 USC § 101 – Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

- A. Claims 33, 34, 49, 50, 65, 66, 81, 82, 97, 98, 113, 114, 129, 130, 145, 146, 161, 162, 177, 178, 193, 194, 209, 210, 225, 226, 241, 242, 257 and 258 are rejected under the judicially created doctrine of

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double patenting over claims 1-5, 7-11 and 14 of U. S. Patent No. 5,932,540 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: the claims of the patent recite isolated polypeptides comprising either a mature form of SEQ ID NO:2, 4, or those of ATCC No. 75968 or 97149, a proprotein of SEQ ID NO:2, 4, or those of ATCC No. 75968 or 97149, those comprising residues 71-396, 47-396, 24-396, 1-396 and -23-396 of SEQ ID NO:2 and a fragment of at least 30 contiguous amino acids of SEQ ID NO:2, or encoded by ATCC No. 75968 or 97149. The claims of the application recite isolated polypeptides which are at least 90% or 95% of the mature, or proprotein forms of SEQ ID NO:2, 4, ATCC No. 75968 or 97149, as well as those comprising residues 71-396, 47-396, 24-396, 1-396 and -23-396 of SEQ ID NO:2 and a fragment of at least 30 contiguous amino acids of SEQ ID NO:2, or encoded by ATCC No. 75968 or 97149. The claims of the present application would encompass those of the patent. These claims are not statutory double patenting since the present application, unlike the patent, recites that the polypeptides must bind a specific antibody.

There is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

B. Claims 33, 34, 49, 50, 65, 66, 81, 82, 97, 98, 113, 114, 129, 130, 145, 146, 161, 162, 177, 178, 193, 194, 209, 210, 225, 226, 241, 242, 257 and 258 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over at least claims 33-44, 53-64, 73-84, 93-104, 113-124, 133-156, 165-176, 185-196, 2-5-216, 225-236, 245-256, 265-276, 285-296, 305-317, 326-338, 347-358, 367-378, 387-398, 407-418 and 427-438 of copending Application No. 09/219,442. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are claiming common subject matter, as follows: the claims of the 09/219,442 application recite isolated polypeptides comprising either a mature form of SEQ ID NO:2, 4, or those of ATCC No. 75968 or 97149, a proprotein of SEQ ID NO:2, 4, or those of ATCC No. 75968 or 97149, those comprising residues 71-396, 47-396, 24-396, 1-396 and -23-396 of SEQ ID NO:2 and a fragment of at least 30 contiguous amino acids of SEQ ID NO:2, or encoded by ATCC No. 75968 or 97149. The claims of the present application recite isolated polypeptides which are at least 90% or 95% of the mature, or proprotein forms of SEQ ID NO:2, 4, ATCC No. 75968 or 97149, as well as those comprising residues 71-396, 47-396, 24-396, 1-396 and -23-396 of SEQ ID NO:2 and a fragment of at

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least 30 contiguous amino acids of SEQ ID NO:2, or encoded by ATCC No. 75968 or 97149. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

C. Claims 33, 34, 49, 50, 65, 66, 81, 82, 97, 98, 113, 114, 129, 130, 145, 146, 161, 162, 177, 178, 193, 194, 209, 210, 225, 226, 241, 242, 257 and 258 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-24, 46-74 of copending Application No. 09/935,726. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: the claimed polypeptide comprising various fragments of SEQ ID NO:2 and 4, such as 30 contiguous amino acids, as well as proteins having a specific % identity to these sequences. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

D. Claims 33, 34, 49, 50, 65, 66, 81, 82, 97, 98, 113, 114, 129, 130, 145, 146, 161, 162, 177, 178, 193, 194, 209, 210, 225, 226, 241, 242, 257 and 258 are provisionally rejected under the judicially created doctrine of double patenting over claim 46 of copending Application No. 08/465,968. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: the presently claimed polypeptide comprising at least 30 contiguous amino acids of SEQ ID NO:2 reads on residues 85-165 of SEQ ID NO:2, as claimed in the '968 application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

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E. Claims 33, 34, 49, 50, 65, 66, 81, 82, 97, 98, 113, 114, 129, 130, 145, 146, 161, 162, 177, 178, 193, 194, 209, 210, 225, 226, 241, 242, 257 and 258 are provisionally rejected under the judicially created doctrine of double patenting over claims 10-18 of copending Application No. 09/623,725. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: the presently claimed polypeptide comprising at least 30 contiguous amino acids of SEQ ID NO:2 reads on 95% identity to N- and C-terminal deletion mutants of SEQ ID NO:2, as claimed in the '725 application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

F. Claims 33-272 are provisionally rejected under the judicially created doctrine of double patenting over claims 22-89 of copending Application No. 09/107,997. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: the presently claimed polypeptide comprising SEQ ID NO:2 and methods of using those proteins, including for the treatment of angiogenesis. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

G. The Examiner brings to Applicants' attention that claims 33, 34, 49, 50, 65, 66, 81, 82, 97, 98, 113, 114, 129, 130, 145, 146, 161, 162, 177, 178, 193, 194, 209, 210, 225, 226, 241, 242, 257 and 258 may be provisionally rejected under the judicially created doctrine of double patenting over one or more claims of copending Application No. 10/060,523. Application 10/060,523 as a divisional of the present application, 09/879,225. Upon performing a search of claimed SEQ ID NO:4 of the present application, Application 10/060,523 was identified as containing a sequence which is 100% identical to this sequence. However, Application 10/060,523 was not available to the Examiner at the time this Office Action was written. Applicants are hereby informed that a provisional double patenting rejection may be made in a subsequent Office Action.

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H. The Examiner brings to Applicants' attention that claims 33, 34, 49, 50, 65, 66, 81, 82, 97, 98, 113, 114, 129, 130, 145, 146, 161, 162, 177, 178, 193, 194, 209, 210, 225, 226, 241, 242, 257 and 258 may be provisionally rejected under the judicially created doctrine of double patenting over one or more claims of copending Application No. 10/084,488. Upon performing a search of claimed SEQ ID NO:4 of the present application, Application 10/084,488 was identified as containing a sequence which is 100% identical to this sequence. However, Application 10/084,488 was not available to the Examiner at the time this Office Action was written. Applicants are hereby informed that a provisional double patenting rejection may be made in a subsequent Office Action.

I. The Examiner brings to Applicants' attention that claims 33, 34, 49, 50, 65, 66, 81, 82, 97, 98, 113, 114, 129, 130, 145, 146, 161, 162, 177, 178, 193, 194, 209, 210, 225, 226, 241, 242, 257 and 258 may be provisionally rejected under the judicially created doctrine of double patenting over one or more claims of copending Application No. 10/127,551 (see claims 69-79 and 83-85). Application 10/127,551 was identified as containing sequences which are 100% identical to both SEQ ID NO:2 and 4. However, no election has been made in Application 10/127,551 at this time. Applicants are hereby informed that a provisional double patenting rejection may be made in a subsequent Office Action.

4. Claim Rejections - 35 USC § 112, first paragraph – enablement

A. Claims 97-192 remain rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 3-4 of the Office Action dated 11/23/01. Applicants do disclose in the Preliminary Amendment, filed 7/18/2000, that ATCC Deposits 75698 and 97149 are maintained under the terms of the Budapest Treaty and will be made available to a patent office signatory to the Budapest Treaty. However, Applicants have not disclosed that all restrictions on the availability to the public of the deposited material so deposited will be irrevocably removed upon the granting of a patent.

B. Claims 33-272 remain rejected for the reasons already of record on pages 4-5 of the Office Action dated 11/23/01. The Examiner apologizes for suggesting that the Applicants added the phrase "wherein said isolated protein specifically binds an antibody that specifically binds SEQ ID NO:2 or 4. However, upon further consideration, the breadth is still excessive with regard to Applicants claiming any isolated protein which is at least 90% identical to the mature or proprotein form of SEQ ID NO:2 or 4, which comprises at least 30 contiguous amino acids of the mature or proprotein form of SEQ ID NO:2 or 4, or which are 90% identical to only a portion of SEQ ID NO:2 (i.e. amino acid residues 71-396, 47-396 and

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24-396). Other than SEQ ID NO:2 and 4, Applicants have not provided any guidance or working examples as to which amino acid residues are required in order to produce a functional VEGF-2 protein, or what the function is of a protein which can be as small as 30 amino acid residues of SEQ ID NO:2 or 4, regardless of whether or not it binds the antibody recited in the claim. Furthermore, it is not predictable to the artisan which critical residues of SEQ ID NO:2 or 4 would be required to produce a functional protein other than that of SEQ ID NO:2 or 4. the fact that a protein, or protein fragment, binds an antibody does not demonstrate that the protein is functional, and does not allow the artisan to make a functional protein.

In summary, the breadth of the claims is excessive with regard to Applicants claiming all proteins which are "at least 90%" identical to SEQ ID NO:2, 4 (ATCC No. 75698 and 97149). In addition, Applicants provide no guidance or working examples of how to use said peptides, such as peptides of amino acids 24-396, 47-396 and 71-396, or fewer, of SEQ ID NO:2, or of at least 30 contiguous amino acids of SEQ ID NO:2, 4 (or to ATCC No. 75698 and 97149) which retain the claimed biological function. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to make a peptide smaller than the full-length protein which is able to retain biological activity, leads the Examiner to maintain that undue experimentation is necessary to practice the invention as claimed.

5. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 33-272 remain rejected for the reasons already of record on pages 6-7 of the Office Action dated 11/23/01. The Examiner apologizes for suggesting that the Applicants added the phrase "wherein said isolated protein specifically binds an antibody that specifically binds SEQ ID NO:2 or 4. However, upon further consideration, written description is still lacking with regard to any isolated protein which is at least 90% identical to the mature or proprotein form of SEQ ID NO:2 or 4, which comprises at least 30 contiguous amino acids of the mature or proprotein form of SEQ ID NO:2 or 4, or which are 90% identical to only a portion of SEQ ID NO:2 (i.e. amino acid residues 71-396, 47-396 and 24-396). Applicants have only provided adequate written description for the proteins of SEQ ID NO:2 and 4. The specification and claims do not indicate what distinguishing attributes are shared by the members of this genus other than SEQ ID NO:2 and 4. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although these types of changes are routinely done in the art, the specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge

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and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:2, 4 (ATCC No. 75698 and 97149), alone are insufficient to describe the genus.

B. Claims 33-64, 97-128 recite a **“mature form of a polypeptide.”** Claims 65-96, 129-160 recite a **“proprotein form of a polypeptide.”** However, the instant specification fails to describe that portion of a protein which is the “mature” portion, or what constitutes a “proprotein.” Applicant is claiming a very specific species which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The structure of a “mature form of a polypeptide” cannot be predicted on the basis of the amino acid sequence of the entire protein since the protein may be proteolytically cleaved in vivo, as well as being differentially processed based on which in tissue the protein is expressed. The claims are directed to a species of protein, the structure of which cannot be determined or predicted from full-length amino acid sequence and the specification does not evidence isolation or conception of the structure of the “mature form of a polypeptide,” or the “preprotein form.” Therefore, the specification does not provide an adequate written description of a mature protein, or preprotein form and thus the claimed invention, to the extent that it reads upon mature protein or proprotein was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

6. Claim Rejections - 35 USC § 112, second paragraph

A. The rejection of all claims under 35 USC 112, second paragraph, regarding “first protein” and “second protein” has been withdrawn since Applicants have removed these terms from the claims.

B. The rejection of all claims under 35 USC 112, second paragraph, regarding “mature” and “proprotein” has been withdrawn in view of Applicants arguments that page 11, lines 15-21 of the specification define these terms.

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Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

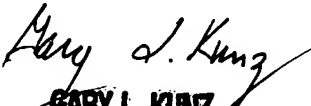
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.

Patent Examiner

Group 1600

August 12, 2002


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